MAIL STOP APPEAL BRIEF-PATENTS
Attorney Docket: 24948

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:

POPP	Group Art Unit: 1611
Serial No.: 10/617,191	Examiner: Channavajjala, Lakshmi Sarada
Filing Date: July 11, 2003	Confirmation No.: 3528

For: **TOPICAL FORMULATIONS FOR TREATMENT OF SKIN DISORDERS**

REPLY BRIEF

This is in response to the Examiner's Answer mailed December 24, 2008. Pursuant to 37 C.F.R. §41.41(a)(1), a Reply Brief may be filed within two (2) months of the date of the Examiner's Answer. Accordingly, this Reply Brief is timely filed.

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REAL PARTY IN INTEREST

The real party in interest is the assignee, STIEFEL LABORATORIES, INC.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

STATUS OF CLAIMS

Claims 1-25 and 32-37 have been cancelled. Claims 26-31 are pending. Claims 26-31 have been rejected, the rejection thereof is hereby appealed. The claims appealed are reproduced in the Appendix appearing in this paper on page 28.

STATUS OF AMENDMENTS

No claim amendments have been entered since the Official Action dated February 4, 2008 was mailed.

SUMMARY OF CLAIMED SUBJECT MATTER

The presently claimed subject matter relates to a process for preparing a storage-stable topical composition for treating a skin disorder or condition. The presently claimed process requires mixing a benzoyl peroxide intermediate dispersion having a viscosity of 60,000 to 250,000 centipoises (cp) and a clindamycin intermediate solution, such that the final composition has a viscosity of 50,000 to 200,000 cp which is lower than the viscosity of the benzoyl peroxide dispersion before mixing.

The single independent claim 26 on appeal recites "a process for preparing a

storage-stable topical composition for treating a skin disorder or condition, which comprises the steps of: (a) forming at a temperature of about 15 to about 25°C a benzoyl peroxide intermediate dispersion having a viscosity of about 60,000 to about 250,000 cp sufficient to yield a composition which contains between about 2.25% and about 12.5% by weight benzoyl peroxide in the final product; (b) forming at a temperature of about 15 to about 25°C a clindamycin intermediate solution sufficient to yield a composition which contains between about 0.5% and about 1.5% by weight clindamycin active in the final product; and (c) mixing said benzoyl peroxide intermediate dispersion and said clindamycin intermediate solution under conditions sufficient to yield a benzoyl peroxide and clindamycin mixture having a final pH of between about 4.5 to about 5.0, wherein said mixture has a viscosity lower than the viscosity of the benzoyl peroxide intermediate dispersion, wherein the viscosity of the mixture is of about 50,000 to about 200,000 cp, and wherein said composition comprises sufficient inactive ingredients to provide storage stability and effectiveness for a treatment period."

Support for claim 26 may be found throughout the specification and claims as originally filed, for example, at page 8, line 23 through page 9, line 19; page 12, lines 12-16; page 15, lines 2-9; and page 27, line 2 through page 28, line 5.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 26-31 are unpatentable under 35 U.S.C. §103(a) over Baroody et al., U.S. Patent No. 6,117,843.

ARGUMENTS

I: Rejection of Claims 26-31 under 35 U.S.C. § 103(a) as being unpatentable over Baroody et al., U.S. Patent No. 6,117,843

In the Examiner's Answer dated December 24, 2008, the Examiner has maintained her rejection of claims 26-31 under 35 U.S.C. §103(a) as being unpatentable over Baroody et al., U.S. Patent No. 6,117,843, for the reasons set forth in the Answer.

As the basis of the rejection, the Examiner states in relevant part that:

> With respect to the process of preparing the composition, example 24 of Baroody describes separately preparing clindamycin and benzoyl peroxide components and mixing the two. For the claimed storage stability, while instant claims do not specify any time period, Baroody shows that the composition is stable over a long period of time (table 8) or even up to 4 months (example 24 in col. 17, see L 50-53). Further, examples 10-13 also describe the process of mixing clindamycin solution with a suspension of benzoyl peroxide. Baroody does not teach that the final viscosity is lower than the viscosity of benzoyl peroxide dispersion. However, example 24 shows mixing of clindamycin solution with benzoyl peroxide gel to obtain a homogenous gel. It is the position of the Examiner that a mixture of a solution (clindamycin) with a gel (benzoyl peroxide), even though in a final homogenous gel form, implicitly results in a composition of lower viscosity than the initial viscosity of the gel.
>
> Instant claims require that the benzoyl peroxide dispersion has a viscosity of 60,000 to 250,000 cp and that the final viscosity of the mixture has a viscosity lower than the viscosity of the benzoyl peroxide immediate dispersion, wherein the viscosity of the mixture is of about 50,000 to about 200,000 centipoises. Baroody discloses that initial viscosity of benzoyl peroxide is below 90,000 cp, usually in the range of 50,000 to 90,000 and a final viscosity in the range of 70,000 to 120,000 (col. 5, L 57-64). Thus, the viscosity ranges taught by Baroody overlap with the viscosity ranges of the instant claims. In other words, the initial viscosity of 50,000 to 90,000 cp (Baroody) overlap with the instant initial viscosity of 60,000 to 250,000 cp. Likewise the final viscosity 70,000 to 120,000 cp (of Baroody) overlap with that of the instant final viscosity of

50,000 to 200,000 cp. Baroody also recognizes the same factors i.e., pH, viscosity, concentration of the components etc., as result-affective variables that affect the stability of the composition. In particular, Baroody teaches that viscosity achieved with the gelling agent (such as Carbopol) is a function of pH (col. 6, table 3). Thus, while Baroody teaches that the final composition may have a relatively higher viscosity, Baroody states that the mixture of benzoyl peroxide and clindamycin has an increased pH and therefore a higher viscosity (col. 6, L 3-6). Baroody also suggests that a final pH in the range of 4-7 and more particularly in the range of 4.5 to 5.5, so as to achieve a long-shelf life for the composition, up to several months. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention was made to employ benzoyl peroxide suspension of appropriate initial viscosity, and mix with clindamycin solution so as to obtain a composition having an optimum final viscosity because Baroody suggests that the viscosity of the final composition is a function of the pH (table 3), which increases with increasing pH. Baroody also suggests that the optimum range of pH is between 4 and less than 7, more preferably between 4.5 and 5.5 (which is within the claimed range), at which range the viscosity is lower compared to the viscosity achieved at higher pH levels of 6.0 to 7.0 (table 3). While Baroody suggests an initial relatively low and a final relatively high viscosity levels for easy mixing of the two components (col. 5, 40-56), Baroody also suggests that the precise weights, volumes, pH levels and the like are all interdependent and should be carefully selected such that the composition possesses desired characters and that the fully prepared composition is stable for a long period of time i.e., 3 months or longer (col. 7, L 18-30). Accordingly, a skilled artisan would have been able to adjust the initial viscosity of benzoyl peroxide in the claimed range, depending on the amounts of active agents, pH level and the amount of gelling agent with an expectation to achieve a composition of an appropriate viscosity that is stable for long periods of time. While instant claims recite an initial higher viscosity and a final lower viscosity, applicants have not shown the criticality of the initial and final viscosities as a function of stability of the composition. See page 4, line 7 to page 6 line 13.

Appellants, again, respectfully traverse the rejection and incorporate herein by reference in their entirety, all arguments presented in the Appeal Brief filed on August 21, 2008 regarding the patentability of the rejected claims since the Examiner has not established a *prima facie* case of obviousness and any potential *prima facie* case of obviousness, if established, is rebutted in the present application.

To establish a *prima facie* case of obviousness, the Examiner must satisfy three requirements. First, as the U.S. Supreme Court very recently held in KSR International Co. v. Teleflex Inc. et al., 550 U.S. 398 (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. Amgen Inc. v. Chugai Pharm. Co., 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970).

A *prima facie* case of obviousness must also include a showing of the reasons why it would be obvious to modify the references to produce the present claims. Ex parte Clapp, 277 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). The Examiner bears the

initial burden to provide some convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings. Id. at 974.

Further, a *prima facie* case of obviousness can be rebutted if applicants can show "that the art in any material respect taught away from the claimed invention," In re Geisler, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997), or the claimed invention yields unexpectedly improved properties or properties not presented in the prior art. In re Dillon, 919 F.2d at 692-93, 16 USPQ2d at 1901. If a *prima facie* case is made in the first instance, and if applicant comes forward with a reasonable rebuttal, whether buttressed by experiment, prior art reference, or argument, the entire merits of the matter are to be reweighed. In re Piasecki, 745 F.20 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984).

In the present application, appellants argued in the Appeal Brief that a *prima facie* case of obviousness has not been established since a person of ordinary skill in the art would have had no suggestion or motivation to modify the process disclosed by the Baroody et al. reference to arrive at the present claims; any potential *prima facie* case of obviousness with the allegation, if established, is rebutted since Baroody et al. expressly teach away from the presently claimed process; and the presently claimed process provides improved properties or properties not present in the prior art.

However, the entire merits of the matter rebutted by the appellants have not been fairly reweighed in the Examiner's Answer. Instead, the Examiner has maintained the rejection by insisting on her previous views regarding the teachings of Baroody et al. and additionally raising an assertion that a mixture of a "solution" of clindamycin with a "gel" of benzoyl peroxide, even though it is in a final homogenous gel form, implicitly

results in a composition of lower viscosity than the initial viscosity of the gel, relying on Example 24 of Baroody et al.

Appellants submit that the Examiner's assertion results from her erroneous interpretation/review of Baroody et al., her failure to consider Baroody et al. as a whole, including teaching away portions, and her failure to avoid hindsight reasoning in determining the obviousness of the present claims.

A. Baroody et al. Teach Away from the Presently Claimed Process

Appellants argue that the disclosure contained in Baroody et al. substantially teaches away from the presently claimed process.

A *prima facie* case of obviousness can be rebutted if applicant can show "that the art in any material respect taught away from the claimed invention." In re Geisler, 43 USPQ2d 1362, 1365 (Fed. Cir. 1997). A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the application. In re Gurley, 31 USPQ2d 1130 (Fed. Cir. 1994). A reference teaches away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant. United States v. Adams, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966).

Further, portions of a reference arguing against or teaching away from the pending claims must be considered. See Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc., 230 USPQ 416 (Fed. Cir. 1986). Thus, the rule of law clearly requires that the Examiner consider a reference in its entirety in determining the

scope and content of the reference. W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, (Fed. Cir 1983), *cert. denied*, 469 U.S. 851 (1984). The Examiner therefore must acknowledge any disclosure in the reference that teaches away from the presently pending claims. Id.

As argued in the Appeal Brief, Baroody et al. teach away from the presently claimed process. Throughout the specification, in particular in the Description of Preferred Embodiments, Baroody et al. expressly and repeatedly teach the selection of a gelling agent in such a way that the initial viscosity of the benzoyl peroxide suspension is relatively lower while the viscosity of the final product is relatively higher. Furthermore, as a benefit of this selection, Baroody et al. expressly teach that the mixing will be easier and the final topical composition can still possess the desired higher viscosity, gel consistency.

However, the Examiner, ignoring all of these teaching away portions in Baroody et al., asserts that because Baroody et al. teach the same pH range for a stable final composition, a skilled artisan would only be led to optimize the process variables such as the viscosity, which is in turn is a function of pH, and thus stabilize the composition of Baroody et al. See page 13, lines 1-7 of the Answer.

Appellants, however, disagree with the Examiner. The Examiner's assertion makes no sense with regard to the teachings of Baroody et al. Appellants argue that a person of ordinary skill in the art who read the teachings of Baroody et al., particularly the teaching away portions, at the "time of the present invention", would not have been led in the direction of a process resulting in a final composition having a viscosity lower than the viscosity of the benzoyl peroxide intermediate, as required by the present

claims. Instead, the disclosure of Baroody et al. would have led a person of ordinary skill in the art in a direction divergent from the process according to the present claims. The Examiner provided no reason why the skilled artisan who read the Baroody et al. reference as a whole would have ignored the repeated teachings of the viscosities in Baroody et al., namely the teachings at, *inter alia,* col. 3, lines 29-36, col. 4, lines 48-52, col. 5, lines 46-57, col. 5, line 58 through col. 6, line 6, col. 6, lines 3-6 and col. 6, lines 22-25.

The Examiner further asserts in the Answer that appellants' arguments presented in the Appeal Brief with regard to the teaching away portions in Baroody et al., are not persuasive because the present claims do not state how high the initial viscosity should be vs. the final viscosity, as well as because appellants have not provided any evidence as to how the initial and final composition is different in terms of viscosities as compared to that of Baroody et al.

However, appellants argue that these Examiner's requests are not reasonable requests to appellants in view of the presently claimed subject matter. The presently claimed subject matter is not directed to a composition at all, but rather is directed to a process for mixing a clindamycin solution and a benzoyl peroxide suspension such that the viscosity of the final composition is lower than the viscosity of the benzoyl peroxide suspension, as described in the present claims. The cited art discloses a process for the preparation of a topical composition comprising clindamycin and benzoyl peroxide, but teaches away from the relative viscosities of the benzoyl peroxide suspension and the final composition as required in the present claims. Accordingly, the Examiner's request for a further limitation of the viscosity is not reasonable in view of the prior art

disclosure. Since the cited reference does not in any way teach the production of a final composition having a viscosity lower than that of an intermediate benzoyl peroxide dispersion, appellants are not required to present any further claim limitations or additional evidence.

The Examiner also asserts that a skilled artisan reading the disclosure of Baroody et al. would readily understand that, depending on the amount of the ingredients in the final composition and the final pH of the composition, one has to vary the amount of gelling agent in the composition such that the pH remains between 4-7 or even between 4.5-5.5, and accordingly, the viscosity also remains at appropriate levels. See page 14, lines 6-11 of the Answer.

However, appellants again argue that what Baroody et al. expressly teach regarding the gelling agent is that: "the gelling agent ideally will be selected to have a reduced viscosity at the pH of the first component and an increased viscosity at the stage of the final product obtained when the two components are combined." See col. 4, lines 48-52. Baroody et al. further teach that "it can be seen that a beneficial increase in viscosity can be achieved by increasing the pH of the final (combined) product relative to the initial pH of the benzoyl peroxide component containing the gelling agent." See col. 6, lines 22-25. Accordingly, the Examiner's assertion is groundless.

The Examiner has failed to consider Baroody et al. in its entirety, particularly the teaching-away portion noted above. The teachings of the Baroody et al. reference do not represent a mere disclosure of more than one alternative, as described by In re Fulton, 391 F. 3d 1195, 1201, 73 USPQ2d 1141, 1146, nor such insubstantial description, as described by In re Gurley. Rather, Baroody et al. expressly teaches how

to set both the viscosities in the benzoyl peroxide suspension and in the final composition, in order to obtain the beneficial effect of facilitating the mixing of the two components and achieving a gel consistency.

Therefore, the portions in Baroody et al. teaching away from the present claims should have been significantly considered by the Examiner in determining the obviousness of the present claims. The Examiner's assertions in the Answer show her failure to provide such consideration, failing to explain why a person of ordinary skill in the art would have been promoted to modify the process in Baroody et al. in a directly opposite way regarding viscosities, in spite of the teaching-away portions.

As such, appellants argue that Baroody et al. throughout the whole reference teaches away from employing a process of producing a final combined composition having a viscosity lower than the viscosity of the benzoyl peroxide intermediate as required by the present claims. Baroody et al., therefore, would have discouraged a person of ordinary skill in the art from following, practicing, or even attempting the presently claimed process to prepare a storage stable topical composition containing benzoyl peroxide and clindamycin.

B. Erroneous Review of Baroody et al. by the Examiner

In the Examiner's Answer, the Examiner concedes that Baroody et al. do not teach that the final viscosity is lower than the viscosity of the benzoyl peroxide dispersion. However, the Examiner asserts that Example 24 of Baroody et al. shows mixing a clindamycin solution with a benzoyl peroxide gel to obtain a homogeneous gel. Thus, it is the Examiner's position that a mixture of a "solution" of clindamycin with a

"gel" of benzoyl peroxide, even though it produces a final homogenous gel form, implicitly results in a composition of lower viscosity than the initial viscosity of the gel. See page 4, lines 15-19; page 9, lines 13-16; and page 13, lines 18-21 of the Answer.

i. Failure to review of Baroody et al. as a whole

Example 24 of Baroody et al. discloses admixing a clindamycin aqueous solution with pH 6.25 and a benzoyl peroxide aqueous gel with pH 5.4, both of which are separately prepared and kept in a kit, to obtain a final composition with stability during storage. Example 24 contains no disclosure regarding the relative viscosities of the benzoyl peroxide gel and the final compositions during preparation. Example 24 however discloses that: "[A]bout 30 grams of an aesthetically pleasing, viscous white gel was produced containing about 5.25% benzoyl peroxide and about 1.2% clindamycin, with a pH of between 5.5 and 4.5 during the shelf life". (Emphasis added) See col. 17, lines 47-50.

Regarding the relative viscosities of the benzoyl peroxide aqueous gel and the final viscous white gel prepared in Baroody Example 24, appellants further note that Baroody et al. expressly teach that the final compositions disclosed therein beneficially has an increased viscosity relative to the viscosity of the benzoyl peroxide component at, *inter alia,* col. 3, lines 29-36, col. 4, lines 48-52, col. 5, lines 46-57, col. 5, line 58 through col. 6, line 6, col. 6, lines 3-6 and col. 6, lines 22-25, as follows:

> [A]dditionally, by properly selecting the gelling agent, the initial viscosity of the benzoyl peroxide suspension (at the suspension pH) may be relatively low, while the viscosity of the final product (at the product pH), can be relatively high to provide a desired gel consistency. Thus, the components may be easily combined by a pharmacist to provide a gel having a pleasing

consistency and texture for use by the patient. (Emphasis added) See at col. 3, lines 29-36.

[T]he gelling agent ideally will be selected to have a reduced viscosity at the pH of the first component and an increased viscosity at the stage of the final product obtained when the two components are combined. (Emphasis added) See at col. 4, lines 48-52.

[B]y properly selecting the nature of the gelling agent and the pH of the benzoyl peroxide component, the benzoyl peroxide component itself may be maintained at a relatively low viscosity while the final topical composition (which is at a different pH) will have a relatively higher viscosity. In this way, mixing of the two components to form the topical composition is facilitated (i.e. the lower viscosity of the benzoyl peroxide component makes the combination and mixing with the clindamycin component easier) while the final topical composition can still possess the desired higher viscosity, gel consistency. (Emphasis added) See at col. 5, lines 46-57.

[P]referably, the viscosity of the benzoyl peroxide component will be below about $9x10^4$, usually being in the range from $5x10^4$ cp to $9x10^4$, more preferably being in the range from $6.5x10^4$ cp to $8.5x10^4$ cp, while the viscosity of the final topical composition product will be in the range from $7x10^4$ cp to $12x10^4$ cp, more preferably being in the range from $8x10^4$ cp to $10x10^4$ cp. These viscosities may be achieved using the polymeric gelling agents, as described above, and a benzoyl peroxide component having a pH in the range from 3.5 to 7.0, preferably in the range from 4.0 to 5.0. The pH may be adjusted by the addition of a pharmaceutically acceptable buffer or base, such as potassium hydroxide. When the benzoyl peroxide component is combined with the clindamycin component, the resulting combined product will have an increased pH resulting in enhanced viscosity within the range set forth above. (Emphasis added) See at col. 5, line 58 through col. 6, line 6.

[T]hus, it can be seen that a beneficial increase in viscosity can be achieved by increasing the pH of the final (combined) product relative to the initial pH of the benzoyl peroxide component containing the gelling

agent. (Emphasis added) See at col. 6, lines 22-25

Accordingly, Example 24 of Baroody et al. would have been viewed by a person of ordinary skill in the art, taking into account the detailed disclosures in the same reference as above, as teaching that the final composition is beneficially prepared to have a relatively higher viscosity than that of the benzoyl peroxide component within the pH range as disclosed in Example 24. Given the detailed and repeated teachings in Baroody et al., as above, regarding the relative viscosities of the benzoyl peroxide components and the final combined composition, a person of ordinary skill would have had no reason to view Example 24 of Baroody et al. as teaching relative viscosities that are exactly opposite to those disclosed throughout the Baroody et al. reference. This is in direct contrast to the Examiner's assertions in the Answer.

The Examiner is respectfully reminded that the prior art taken as a whole must be considered. Also, the reference teachings are to be viewed as they would have been viewed by one of ordinary skill. Kimberly-Clark v. Johnson & Johnson, 745 F.2d 1437, 1454, 223 USPQ 603, 614 (Fed. Cir. 1984); In re Mercier, 515 F.2d 1161, 1165, 185 USPQ 774, 778 (CCPA 1975). It is impermissible within the framework of §103 to pick and choose from any one reference only so much of the reference as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. In re Wesslau, 353 F.2d at 241, 147 USPQ at 393.

Accordingly, appellants argue that the above Examiner's assertion should be regarded as resulting from her erroneous separation of Example 24 from the whole

teachings of Baroody et al., from her failure to consider the prior art as a whole, and from her failure to view the teachings of Example 24 as they would have been viewed by a person of ordinary skill as required by Kimberly-Clark v. Johnson & Johnson, Id.

Further, appellants additionally argue that, for the Examiner's assertion to be reasonable, it should also be reasonable to state that in all the processes disclosed in Baroody et al., particularly in Examples 10-13 disclosing admixing the clindamycin solution of Example 1 with the benzoyl peroxide suspensions of Example 5, Example 6 and Example 7, respectively, the resulting final compositions should have a reduced viscosity than the benzoyl peroxide intermediate suspension because all of the clindamycin "solutions" would have a lower viscosity than the benzoyl peroxide "gels".

However, this position is contradictory on its face to the detailed disclosure in Baroody et al. regarding the relative viscosities. Also, this position is contradictory to the Examiner's other assertions presented in the Answer based on the pH disclosure in Baroody et al., particularly the assertion relying on Table 3 of Baroody et al. In particular, based on the Examiner's arguments regarding the mixing of a "solution" and a "gel", the viscosity of the final composition in Examples 10-13 should be lower than the benzoyl peroxide suspension. However, the viscosity of these same final compositions should be higher according to the Examiner's assertion based on the pH disclosure in Table 3. That is to say, the pH values of the benzoyl peroxide suspensions of Examples 5-7 are pH 4.5, pH 4.7 and pH 4.3, respectively, while the pH values of the final compositions in Examples 10-13 would be expected to be 4.5-5.5. At this range, the viscosity of the final compositions is expected to be higher according to Table 3 of Baroody et al., as indicated by the Examiner in the Answer.

Accordingly, again, appellants argue that the above Examiner's assertion results from the erroneous extraction of Example 24 only from the whole teachings of Baroody et al., excluding the other teachings necessary to a full appreciation of Baroody et al. by a person of ordinary skill in the art. Again, as required by In re Wesslau, Id., it is impermissible within the framework of the nonobviousness section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.

ii. Hindsight

Further, the only reason that can explain why a person of ordinary skill would have viewed Example 24 as implicitly teaching the same process as the present claims, in spite of the opposite teachings in the same reference, is the Examiner's erroneous hindsight reasoning. As section 103(a) clearly states, the Baroody et al. reference could not have taught the present claims "at the time of invention", rather than at the time the Examiner examines the present application with the help of the knowledge obtained from the present application. Appellants argue that "at the time of the present invention", what the Baroody et al. reference taught as a whole is the preparation of a stable topical composition comprising clindamycin and benzoyl peroxide by simply mixing a clindamycin solution and a benzoyl peroxide suspension in such a way that the final mixed composition beneficially has an increased higher viscosity relative to the reduced viscosity of the benzoyl peroxide suspension, as Baroody et al. expressly disclose throughout the reference. Accordingly, appellants respectfully submit that the Examiner's assertions in the Examiner's Answer regarding Example 24 should be

considered as resulting from the Examiner's erroneous application of hindsight knowledge obtained from the present application.

Accordingly, appellants respectfully request reversal of the Examiner's decision.

C. No Suggestion or Motivation to Modify the Process in Baroody et al. to Reach the Presently Claimed Process

One way of avoiding hindsight in determining (non)obviousness of pending claims, is to look to whether there is a teaching, suggestion or motivation to modify the prior art teachings to arrive at the pending claims. Obviousness can be established by combining or modifying the teachings of the prior art to produce the pending claims where there is some teaching, suggestion, or motivation to do so. In re Kahn, 441 F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006). If the proposed modification would render the prior art being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). If the proposed modification or combination of the prior art would change the principle of operation of the prior art being modified, the teachings of the references are not sufficient to render the claims *prima facie* obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Further, in KSR, *supra*, the court also requires an "apparent reason" to combine the known elements in the fashion claimed by the application at issue, or a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the pending claims do.

The Examiner asserts in the Answer that: "... because Baroody suggests that the viscosity of the final composition is a function of the pH (table 3), which increases with increasing pH", and "... because Baroody states that the precise weights, volumes, pH levels and the like are all interdependent and should be carefully selected such that the composition possesses desired characters and that the fully prepared composition is stable for a long period of time", it would have been obvious for one of ordinary skill in the art "at the time the instant invention was made" to mix a benzoyl peroxide suspension of appropriate initial viscosity with a clindamycin solution so as to obtain a composition having an optimum final viscosity. For the same reason, the Examiner further asserts that a skilled artisan would have been able to adjust the initial viscosity of benzoyl peroxide in the claimed range.

However, appellants argue that the present claims are not directed to a stable topical composition having an optimal viscosity, nor to a process for the preparation of such a topical composition simply by mixing a clindamycin solution and a benzoyl peroxide suspension. As clearly described in the present claim 1, the present claims are directed to a process for preparing a storage-stable topical composition by mixing a benzoyl peroxide intermediate dispersion having a viscosity of 60,000 to 250,000 centipoises (cp) and a clindamycin intermediate solution, such that the final composition has a viscosity of 50,000 to 200,000 cp which is lower than the viscosity of the benzoyl peroxide dispersion before mixing. The prior art does not in any way meet the limitation "wherein said mixture has a viscosity lower than the viscosity of the benzoyl peroxide intermediate dispersion" as required by the present claim 1. As such, the cited reference does not teach the present claims, and in the same way, does not fall within

the scope of the present claims. Accordingly, the Examiner's assertion that it would be obvious to adjust the optimal viscosities of the final composition and the intermediate benzoyl peroxide, has nothing to do with the obviousness of the presently claimed process.

In addition, for the same reason, the disclosure that "the precise weights, volumes, pH levels and the like are all interdependent and should be carefully selected such that the composition possesses desired characters and that the fully prepared composition is stable for a long period of time" in Baroody et al. should be read as teaching that "the precise weights, volumes, pH levels and the like should be carefully selected such that the composition possesses desired characteristics (*as disclosed in this reference*) ... ", from the view point of a person of ordinary skill in the art who read the Baroody et al. reference. The "desired characteristics" therein should be viewed as teaching that "the lower viscosity of the benzoyl peroxide component makes the combination and mixing with the clindamycin component easier while the final topical composition can still possess the desired higher viscosity, gel consistence" as expressly disclosed in the foregoing col. 5 and col. 6 of Baroody et al. See col.5, lines 51-57 of Baroody et al. This disclosure implicitly provides evidence that the Baroody et al. compositions would be harder to mix if the viscosities were reversed, as requested by the Examiner.

As such, those portions in Baroody et al. consistently cited by the Examiner do not provide any teaching, suggestion or motivation to arrive at the present claims, nor an apparent reason as the law requires for a *prima face* case of obviousness.

The Examiner further asserts that Baroody et al. "states the viscosity may be relatively low and high, suggesting that it may be varied." See page 8, lines 21-22 of the Answer. However, as appellants constantly point out, Baroody et al. clearly and expressly teach that the final combined composition beneficially has an increased higher viscosity relative to the reduced viscosity of the benzoyl peroxide suspension, rather than suggesting that the viscosity may be varied. Nowhere do Baroody et al. teach or suggest that the viscosities may be varied in such a way that they can even be opposite to the disclosures in the Descriptions of Preferred Embodiments. The Examiner's interpretation is possible only with the help of knowledge or bias obtained from the present application, which is absolutely unallowable in determining the obviousness of the present claims.

As such, reading the teachings of Baroody et al. as a whole, without hindsight, a person of ordinary skill would have reached the conclusion that there is no suggestion or motivation to modify the process in Baroody et al. to arrive at the present claims. In this respect, the Examiner has failed to establish a *prima facie* case of obviousness.

Accordingly, appellants respectfully request reversal of the Examiner's decision.

D. Unexpected Results and Advantages of the Presently Claimed Process

Appellants additionally assert that the presently claimed process has unexpected results and advantages as compared to the process disclosed in the Baroody et al. reference, and that this rebuts any alleged *prima facie* case of obviousness.

Rebuttal evidence may include evidence that the pending claims yield

unexpectedly improved properties or properties not present in the prior art. In re Dillon, 919 F.2d at 692-93, 16 USPQ2d at 1901. Further, rebuttal evidence and arguments can be presented in the specification, In re Soni, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir. 1995), by counsel, In re Chu, 66 F.3d 292, 299, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995), or by way of an affidavit or declaration under 37 CFR 1.132, e.g., Soni, 54 F.3d at 750, 34 USPQ2d at 1687; In re Piasecki, 745 F.2d 1468, 1474, 223 USPQ 785, 789-90 (Fed. Cir. 1984).

The Baroody et al. reference presents, as a benefit or effect of the process disclosed therein, the facilitation of mixing two components by selecting a gelling agent to have a lower viscosity in a benzoyl peroxide suspension and a higher viscosity in a final composition. Baroody et al. further presents the storage stability of the topical composition prepared according to this procedure for at least one month, for two months, and for three months or longer. See, Baroody et al. col. 5, lines 51-57 and col. 7, lines 25-30. Further, the combining of the benzoyl peroxide suspension and the clindamycin solution in the Baroody et al. reference is presented to be done prior to use by a pharmacist. See, id. col. 3, lines 26-36.

As argued in the Appeal Brief, in the presently claimed process the viscosity of the final composition is lower than the viscosity of the benzoyl peroxide intermediate, which is exactly opposite to the teachings of Baroody et al. and thus is not expected to provide the same beneficial effect as presented in Baroody et al. The expected or predictable effect from using viscosities opposite to those disclosed by Baroody et al., as claimed in the present claims, is that it would make the mixing harder, resulting in worse homogeneity of the final composition.

Unexpectedly, however, it has been found that the presently claimed process, where the final viscosity is lower than the viscosity of the benzoyl peroxide intermediate dispersion, provides compositions that are easier to mix together, contain less degradates, and have a greater degree of uniformity than those compositions previously known in the art, including the Baroody et al. composition. See, page 15, lines 4-9, of the present application.

In addition, regarding the storage stability of the composition, Baroody et al. specifically presents experimental data in this regard in Table 8 of Example 17. In Example 17, Baroody et al. describe that after two (2) months storage at room temperature, 90% of the original concentration of clindamycin (1.20% to 1.08%) and 99% of the original concentration of benzoyl peroxide (5.87% to 5.83%) remained in the admixed gel. Accordingly, only relying on this experimental data, the composition in the Baroody et al. reference is considered as remaining stable for two months with 90% of the original clindamycin and 99% of the original benzoyl peroxide.

However, the topical composition prepared according to the presently claimed process has the same amount of clindamycin, i.e., 1.2% of clindamycin. From the Tables 3 and 4 in Example 4 of the present application, it is confirmed that, at 25°C, after three months, the original concentration of clindamycin in the present topical composition remains over 90% (1.24% to 1.13%) and after six months, the original concentration of benzoyl peroxide remains over 99% (i.e., 5.09% to 5.06%). Accordingly, the topical composition prepared according to the presently claimed process has an improved storage stability in comparison to the topical composition in the Baroody et al. reference. These unexpected results provide direct evidence

regarding the non-obviousness of the present claims in view of the Baroody et al. reference.

In addition, the improved stability provided by the compositions prepared according to the presently claimed processes provides pharmacists and other dispensers of medication with a product which no longer requires compounding at the time of dispensing. Because compounding is no longer required, homogeneity is controlled at the point of manufacture, which improves dosing and ultimately compliance. See, page 33, lines 4-12, of the present application.

The Baroody et al. reference, however, does not present these beneficial properties shown in the topical compositions prepared by the presently claimed process. Actually, in the Baroody et al. reference, the compounding or admixture of the two components is done "prior to use" by a pharmacist, and thus, the benzoyl peroxide suspension and the clindamycin solution are maintained as separate components in a kit before the compounding thereof by the pharmacist. See, id. col. 2, lines 64-65 and col. 3, lines 21-22

As such, appellants assert that the presently claimed process has unexpected improved properties or properties not presented in the Baroody et al. reference, as established by In re Dillon. Also, the supporting evidence and arguments can be found in the present specification and the Baroody et al. reference themselves, as permitted by In re Soni.

Accordingly, appellants respectfully submit that any alleged *prima facie* case for obviousness has been rebutted by the unexpected results of the present claims.

CONCLUSION

For the foregoing reasons, appellants respectfully submit that the Examiner's rejection of the presently pending claims 26-31 was erroneous. Accordingly, appellants respectfully request reversal of the Examiner's decision.

The Commissioner is authorized to charge Deposit Account No. 14-0112 for any additional charges in connection with this appeal.

The Examiner is welcomed to contact the undersigned attorney if such contact would be helpful in the further prosecution of this case.

Respectfully Submitted,

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Date: February 20 , 2009

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Appendix A

Claims on Appeal

1 - 25. (Cancelled)

26. (Previously presented) A process for preparing a storage-stable topical composition for treating a skin disorder or condition, which comprises the steps of:

a) forming at a temperature of about 15 to about 25°C a benzoyl peroxide intermediate dispersion having a viscosity of about 60,000 to about 250,000 centipoises sufficient to yield a composition which contains between about 2.25% and about 12.5% by weight benzoyl peroxide in the final product;

b) forming at a temperature of about 15 to about 25°C a clindamycin intermediate solution sufficient to yield a composition which contains between about 0.5% and about 1.5% by weight clindamycin active in the final product; and

c) mixing said benzoyl peroxide intermediate dispersion and said clindamycin intermediate solution under conditions sufficient to yield a benzoyl peroxide and clindamycin mixture having final pH of between about 4.5 to about 5.0,

wherein said mixture has a viscosity lower than the viscosity of the benzoyl peroxide intermediate dispersion, wherein the viscosity of the mixture is of about 50,000 to about 200,000 centipoises, and wherein said composition comprises sufficient inactive ingredients to provide storage stability and effectiveness for a treatment period.

27. (Original) The process of claim 26, wherein said process results in a composition having benzoyl peroxide impurities of not more than about 0.01% by weight.

28. (Original) The process of claim 26, wherein said process results in a

composition having clindamycin degradates of not more than about 0.02% by weight.

29. (Original) The process of claim 26, wherein said process results in a composition having benzoyl peroxide impurities of not more than about 0.01% by weight and clindamycin degradates of not more than about 0.02% by weight.

30. (Original) The process of claim 26, wherein said mixture has a final pH of between about 4.6 to about 4.8.

31. (Original) The process of claim 26, wherein said composition has less water by weight as compared to a topical formulation having one of benzoyl peroxide or clindamycin but not both.

32 – 37. (Cancelled)

Appendix B

Evidence Appendix

NONE

Appendix C

Related Proceedings Appendix

NONE